provided on page B2 in **Exhibit B** attached hereto.

On page 6, replace the paragraph at lines 2-5, with the replacement paragraph in clean form provide on page A6 in **Exhibit A** attached hereto. A marked-up version of the paragraph, with deleted matter in brackets and with added matter underlined, is provided on page B6 in **Exhibit B** attached hereto.

On page 17, replace the first full paragraph, with the replacement paragraph in clean form provided on page A17 in **Exhibit A** attached hereto. A marked-up version of the paragraphs, with deleted matter in brackets and with added matter underlined, is provided on page B17 in **Exhibit B** attached hereto.

In the Claims

Please amend claims 1, 10-14 and 16-20 as marked-up in **Exhibit C** attached hereto, by deleting the bracketed matter and inserting the underlined matter. A clean copy of claims 1, 10-14 and 16-20, as amended, is attached hereto as **Exhibit D**.

REMARKS

Claims 1-20 are pending and presented for examination in the subject application. Applicant has hereinabove amended claims 1, 10-14 and 16-20.

Claims 1, 10-14 and 16-20 have been amended to place the claims in better form for examination, without narrowing the scope of the claimed invention.

Applicant maintains that no new matter is presented by this amendment. Accordingly, Applicant respectfully requests that this Amendment be entered.

Objection To Abstract Of The Disclosure

On page 2 of the December 3, 2002 Office Action, the abstract of the disclosure was objected to.

The Examiner stated that the abstract of the disclosure was objected to because of the use of the term often used in patent claims, e.g., "comprising".

In response, without conceding the correctness of the Examiner's position, but solely to advance prosecution of the subject application, Applicant has amended the abstract of the disclosure.

Accordingly, Applicant respectfully requests that the Examiner withdraw the objection to the abstract of the disclosure.

Objection To The Disclosure

On page 2 of the December 3, 2002 Office Action, the disclosure was objected to.

The Examiner stated the disclosure was objected to because of the following purported informalities: (1) the status of applications Serial No. 08/681,219 or 09/230,111 recited at page 17, lines 7-10 have not been provided; and (2) there is no Seq. ID. No. for sequence GLGF recited at page 2, line 27 of the instant specification. The Examiner further stated that Applicant is requested to check for other Sequences in the specification that do not have ID. Nos. The Examiner stated that appropriate correction is required.

In response, without conceding the correctness of the Examiner's position, but solely to advance prosecution of the subject application, Applicant has amended the disclosure.

Accordingly, Applicant respectfully requests that the Examiner withdraw the objection to the disclosure.

Rejection under 35 U.S.C. §112, first paragraph

On page 2 of the December 3, 2002 Office Action, claims 1-20 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner stated that the specification fails to provide a written description for the claimed method of preparing a protein array with the protein elements either alone or in combination with other elements such as oligonucleotide, DNA, mRNA, sugar. The Examiner further stated that there is no description as to whether the array comprises each of the different elements or form a part of the protein molecule. The Examiner also stated that the description in the specification repeats only what is in the claims and simply states that the array has said other components.

The Examiner stated that it is not readily apparent from the Examples provided therein whether a protein array has been prepared. The Examiner further stated that all of the examples relate to screening a random library and the inhibitory effect of a tripeptide between the Fas-Fap interactions.

Applicant has hereinabove amended the claims to place the claims in better form for examination. Applicant maintains that the claim amendments do not narrow the scope of the claimed invention, but rather clarify the claims. In particular, claims

10-13 have been amended herein to recite that at least one array element also includes an oligonucleotide, messenger RNA, DNA or sugar, respectively. Claims 17-20 have similarly been amended herein.

Applicant maintains that the claimed invention as set forth in the amended claims are fully supported by an adequate written description of the claimed invention.

The subject application describes on, for example, pages 17-25 experiments performed by and/or under the direction and supervision of Applicant. Based on the results of the experiments, which are discussed in the application (for example, at page 22, line 35 through page 23, line 11) as well as in pending U.S. applications nos. 08/681,219 (filed July 22, 1996) and 09/230,111 (filed May 17, 1999) which are incorporated by reference in the subject application, Applicant recognized the advantages of protein-protein interaction as between, on the one hand, a first protein (or polypeptide) which comprises a PDZ domain and, on the other hand, a second protein (or polypeptide) which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH, the amino acid sequence (S/T)-X-(V/I/L)-COOH, wherein each hyphen represents a peptide bond, each parenthesis encloses amino acids which are alternatives to one other, each slash within such parentheses separates the alternative amino acids, and the X represents any amino acid which is selected from the group consisting essentially of alanine, cysteine, aspartic acid, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, glutamine, arginine, serine, threonine, valine, tryptophan and tyrosine.

Applicant further recognized that the protein-protein interaction between the first and second proteins (or polypeptides) may be

harnessed through array processing technologies to keep the proteins in a functionally active state and allow multiple drug screenings under physiological conditions.

As discussed in the application exemplarily at page 14, line 21 through page 16, line 14, a number of different configurations of protein (or polypeptide) arrays may be prepared. For example, each array element may be a microwell in which a protein solution is deposited (see Fig. 14C and page 14, line 30 through page 15, line 5). As another example, each array element may be a gel pad deposited as part of a micromatrix on a glass slide, with the protein solution transferred via a pin-like device to the gel pad (see Fig. 14B and page 15, lines 12-29). Other techniques known in the art may also be used to prepare a protein array.

As pointed out in several parts of the application, the preparation may be an array of polypeptides, which may or may not include one or more array elements which include oligonucleotides, sugars, messenger RNAs, DNAs, and/or other compounds (see, for example, page 11, lines 30-35; page 13, line 21 through page 14, line 1; page 14, lines 11-19).

In addition, it should be noted that "[i]t is now well known that a satisfactory description may be in the claims or any other portion of the originally filed specification" (see MPEP 2163, subsec I, paragraph 2).

Therefore, Applicant maintains that the subject application describes sufficient detail of and adequate support for the claimed invention.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-20 under 35

U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

On page 3 of the December 3, 2002 Office Action, claims 1-20 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Examiner stated that claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. The Examiner further stated that the omitted steps are the intervening steps between (a) and (b) steps. The Examiner also stated that it is not clear as to the conditions that result in a protein-protein interaction after deposition of the first protein and before application of the second protein, especially in the absence of positive recitation in the specification as to the steps. The Examiner further stated that it is not clear whether the alternative tripeptide is applied individually or a library containing the alternative groups.

The Examiner stated that the language "selected from the group comprising" is an improper Markush language. The Examiner suggested that comprising be changed to "consisting". The Examiner further suggested that the twenty amino acid residues be recited.

The Examiner stated that claim 3 broadens base claim 1 with the recitation that the "array is used to screen one or more drug targets". The Examiner further stated that the base claim recites only a method of preparing and not a screening method. The Examiner also stated that there is no recitation in the base claim of a physiological condition.

The Examiner stated that the language in claim 13 of "at least one a sugar" is grammatically incorrect.

The Examiner stated that claims 10-23 and 17-20 are confusing and unclear as to whether each of these compounds form a part of the protein molecule or are separate, discrete components of the protein array, especially in the absence of positive teaching or showing in the specification as to how such array are prepared with these different compounds.

The Examiner stated that the term 'corresponding' PDZ domain in claim 4, within the claimed context, is indefinite as in what manner or what constitutes a corresponding PDZ domain.

The Examiner stated that claim 16 is indefinite as there is inconsistency between the preamble and the body of the claim. The Examiner further stated that the preamble recites a method for preparing a protein array while the body recites a method for making a polypeptide.

In response, without conceding the correctness of the Examiner's position but solely to advance the prosecution of the subject application, Applicant has hereinabove amended claims 1, 10-13 and 16-20 to place the claims in better form for examination, without narrowing the scope of the claimed invention.

Applicant notes that although the Office Action states that claim 1 omits essential steps which are gaps in the recited steps, no such "essential" steps are identified in the Office Action. Applicant maintains that the physiological conditions under which the claimed method may be practiced vary. Therefore contrary to the statement in the Office Action, no essential steps are

omitted from claim 1.

Further, as described in the application (for example, at page 12, lines 15-21), a single first protein may be deposited in each array element or a plurality of first proteins may be deposited in the array. Similarly, one or more second proteins may be deposited in the array.

Regarding claim 3, it should be noted that the claim includes all of the limitations of claim 1. In addition, claim 3 includes a further limitation of the claimed invention to one of many possible uses of the array prepared by the method claimed in claim 1. Threfeore, Applicant maintains that claim 3 cannot be broader than claim 1.

Applicant respectfully submits that the amended claims clearly recite the subject matter Applicant regards to be the invention. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-20 under 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §103(a)

On page 6 of the December 3, 2002 Office Action, claims 1-20 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Doyle ("the Doyle paper") in view of any one of applicant's disclosure of know prior art or Schneider-Mergener ("the Schneider-Mergener paper") or Harris et al. ("the Harris paper").

The Examiner stated that the Doyle paper discloses, at page 1067, a modular PDZ domain that binds to the peptide motif T/S-X-Val at the C-terminus of protein K Channels and NMDA receptor ion channels. The Examiner further stated that the the Doyle paper discloses at page 1072 that Val can be varied with Ile.

The Examiner acknowledged that the Doyle paper does not disclose a method of preparing an array for the PDZ domain with its receptor.

The Examiner stated that the Applicant discloses at page 3, lines 23-34 that a "recent trend in biology, biotechnology and medicine is the use of arrays of immobilized biological compounds in studies of immunoassays and enzymatic reactions. The Examiner further stated that, mass sensing, multianalyte microarray immunoassays have been performed. The Examiner also stated that the use of arrays allows for large scale and high-throughput studies of multiple samples in parallel. The Examiner further stated that integration of microarray technology into the experimental methodology also may increase efficiency in many instances, such as through reducing the volume of samples and reagents required.

The Examiner stated that the Harris paper discloses an array of target proteins to which PDZ containing proteins bind.

The Examiner stated that the Schneider-Mergener paper discloses that an array is a versatile toolbox for a variety of application in proteomics.

The Examiner alleged that it would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare or to format the PDZ domains of the Doyle paper into an array since forming a compound into an array will provide a high-throughput screening for a desired receptor or ligand, as taught by Applicant's disclosure and the Schneider-Mergener paper. The Examiner further stated that this is evident from the teachings of the Harris paper, which discloses an array of target

receptors for the PDZ domain.

The Examiner alleged that claim 14 is obvious over the teachings of the Doyle paper at page 1067 disclosing the different corresponding PDZ domain.

The Examiner alleged that claim 16 is obvious over the teaching of the Doyle paper as to the proteins or polypeptides of PDZ domain at page 1067, col. 2.

Applicant maintains that the Doyle paper, the Schneider-Mergener paper and the Harris paper do not render obvious the claimed invention. The claimed invention is patentable over the Doyle paper, the Schneider-Mergener paper and the Harris paper for at least the following reasons.

The Doyle paper, as understood by Applicant, relates to the crystal structures of a complexed and peptide-free membrane protein-binding domain. The Doyle paper states that the X-ray crystallographic structures of the third PDZ domain from the synaptic protein PSD-95 reveal that a four-residue C-terminal stretch (i.e. X-Thr-/Ser-X-Val-COO^-) engages the PDZ domain through antiparallel main chain interactions with a β sheet of the domain. The Office Action acknowledged that the Doyle paper fails to recognize the benefits of protein-protein interaction as between, on the one hand, a first protein (or polypeptide) which comprises a PDZ domain and, on the other hand, a second protein (or polypeptide) which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH, and harnessing the protein-protein interaction, as provided by the claimed invention, through protein (or polypeptide) array processing technologies to keep the proteins in a functionally active state and allow multiple drug screenings under physiological conditions.

The Schneider-Mergener paper, as understood by Applicant, relates to synthetic peptide and protein domain arrays prepared by applying a SPOT technology for parallel synthesis of peptides. The Schneider-Mergener paper, like the Doyle paper, fails to disclose or suggest the benefits of protein-protein interaction as between, on the one hand, a first protein (or polypeptide) which comprises a PDZ domain and, on the other hand, a second protein (or polypeptide) which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH. The Schneider-Mergener paper and the Doyle paper do not supply the requisite motivation for combining or adapting their teachings, without using the claimed invention as a roadmap in hindsight.

The Harris paper, as understood by Applicant, relates to a survey of recent research of the structure and and function of PDZ domains for their roles in transport, localization and assembly of multi-protein signaling complexes. Although the Harris paper states that PDZ domains can be used in combination to bind an array of target proteins or to oligomerize into branched networks, Applicant finds no teaching or suggestion in the Harris paper of the benefits of protein-protein interaction as between, on the one hand, a first protein (or polypeptide) which comprises a PDZ domain and, on the other hand, a second protein (or polypeptide) which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH.

Therefore, there is not the required motivation for combining the Doyle paper, the Schneider-Mergener paper and the Harris paper in the manner suggested in the Office, unless the claimed invention is used to guide the hindsight reconstruction as performed in the Office Action.

It should also be noted that even though the general state of the art in array processing is mentioned in the Background section of the subject application, the array processing art does not remedy the deficiencies of the Doyle paper, the Schneider-Mergener paper and the Harris paper, to supply the required motivation.

Therefore, it is respectfully submitted the claimed invention is not rendered unpatentable by the prior art.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-20 under 35 U.S.C. §103.

Supplemental Information Disclosure Statement

This Supplemental Information Disclosure Statement is submitted under 37 C.F.R. §1.97(c)(2) to supplement the Information Disclosure Statements filed on June 6, 2002.

In accordance with the applicant's duty of disclosure under 37 C.F.R. §1.56, Applicant directs the Examiner's attention to the following references which are also listed on the Form PTO-1449 attached hereto as **Exhibit 1** and copies of which are attached hereto as **Exhibits 2-5**:

U.S. Patent Application Publication No. 2002/0058607A1, published May 16, 2002, Sato et al. (Exhibit 2);

Japanese Patent Application Hei 9-512598, published September 7, 1999, including English-language machine translation (Exhibit 3);

Mendoza, L.G., et al. (1999) "High-throughput microarray-based enzyme-linked immunosorbent assay (ELISA)",

Biotechniques, 27(4)778-780, 782-786, 788 (Exhibit 4); and

Rowe, C.A., et al. (1999) "An array immunosensor for simultaneous detection of clinical analytes", Analytical Biochemistry, 71(2):433-439 (Exhibit 5).

It should be noted that Japanese Patent Application Hei 9-512598 is a Japanese counterpart of PCT International Publication No. WO 97/11091 which was submitted with the Information Disclosure Statement filed on June 6, 2002. It should also be noted that the the Mendoza and Rowe references were also cited in the June 6, 2002 Information Disclosure Statement, although copies of the Mendoza and Rowe references were not available at the time and therefore were not enclosed with the June 6, 2002 Information Disclosure Statement.

This Information Disclosure Statement is filed pursuant to 37 C.F.R. §1.97(c)(2), after the mailing date of a first Office Action, but before a Final Office Action, a Notice of Allowance or an action that otherwise closes prosecution in the application. The fee under 37 C.F.R. §1.17(p) for filing an Information Disclosure Statement pursuant to 37 C.F.R. §1.97(c)(2) is ONE HUNDRED AND EIGHTY DOLLARS ($180.00). Authorization is hereby given to charge the ONE HUNDRED AND EIGHTY DOLLARS fee under 37 C.F.R. §1.17(p) to Deposit Account No. 03-3125.

In view of the amendments to the claims and remarks hereinabove, Applicant maintains that claims 1-20 are now in condition for allowance. Accordingly, Applicant earnestly solicits the allowance of claims 1-20.

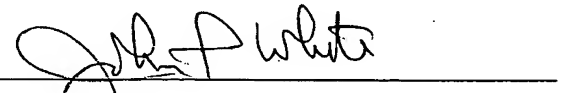
If a telephone interview would be of assistance in advancing

prosecution of the subject application, Applicant's undersigned attorney invites the Examiner to telephone him at the telephone number provided below.

If a petition for an extension of time is required to make this response timely, this paper should be considered to be such a petition, and the Commissioner is authorized to charge the requisite fees to our Deposit Account No. 03-3125.

No fee, other than the $180.00 fee under 37 C.F.R. §1.17(p) for the Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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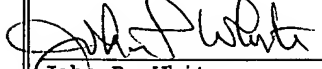
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



3/3/03

John P. White **Date**
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